Assiut Vet. Med. J. Vol. 43 No. 86, July 2000

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YOHIMBINE AND TOLAZOLINE ANTAGONISM OF XYLAZINE CNS-DEPRESSION IN THE CAMEL

(With 3 Figures)

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(Received at 13/6/2000)

يوهمبين و تولازولين لمعالجة الأثر التثبيطي لعقار زيلازين على الجهاز العصبي المركزي في الجمال

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أجريت هذه الدراسة على ثلاثة مجموعات من ذكور الجمال (عمر ٨-١٢ شهر ووزن ٢٥٠- ٣٠٠ كج) ، تم حقن الحيوانات بعقار زيلازين بجرعة ٠،٥ ملج/ كج في الوريد و بعد ١٠ دقائق حقنت حيوانات حيوانات المجموعة الاولى ٥ مل من محلول الملح الفسيولوجي وريديا و المجموعة الثانية تولازولين ١،٥ ملج / كج بالوريد و المجموعة الثالثة حقنت يوهمبين ٠،٢٥ . ملج / كج. بدأ اللاثر التثبيطي للجهاز العصبي المركزي يظهر خلال ٣ دقائق من حقن عقار زيلازين وكان التركيز العميق والتسكين واضحا خلال ٧ دقائق واستمر حتى ٢٥-٣٠ دقيقة. استمرت الحيوانات هادئة حتى ٦٠- ٧٠ دقيقة من حقن عقار زيلازين. أمكن معالجة التأثير التثبيطي لعقار زيلازين على الجهاز العصبي المركزي باستخدام عقارى يوهمبين وتولازولين خلال ٢-٧ دقائق. بينما امكن معالجة بطء القلب وانخفاض معدل التنفس خلال ١٠ دقائق أخذ الكرش ٨٠ دقيقة ليكون التحسن في حركته واضحا. يمكن إستخدام أى من عقارى تولازولين أو يوهمبين لمعالجة التأثير التثبيطي للجرعات الزائدة من عقار زيلازين في الجمال.

SUMMARY

Three groups of camel calves of 4 animals each, were injected xylazine by the intravenous route at a dose rate of 0.5 mg/kg body weight to induce CNS depression. Ten minutes later group 1 animals were injected iv, each, with 5ml saline, group 2 were injected iv with 1.5 mg/kg tolazoline while group 3 camels were injected iv with 0.25 mg/kg yohimbine. The signs of CNS depression, the respiratory rate, heart rate and ruminal movements were recorded for each animal before and after xylazine injection, and after yohimbine and tolazoline administration. CNS depression began within three minutes after the intravenous

administration of xylazine in camels and deep sedation and analgesia where apparent within 7 minutes and lasted for 25 to 30 minutes. The animals remained calm till 60 to 70 minutes. Tolazoline and yohimbine could reverse xylazine CNS depression in camels within 2 to 7 minutes. While xylazine produced bradycardia and decrease in the respiratory rate were reversed within 10 minutes after tolazoline and yohimbine administration, the improvement of rumen motility took 80 minutes to be apparent. Yohimbine effect at the dose studied was more pronounced than tolazoline to reverse the depressant effect of xylazine. Both tolazoline and yohimbine would be useful as antidot for xylazine overdose in camels.

Key words: Yohimbine & Tolazoline, Xylazine, Cns-Depression, Camel.

INTRODUCTION

Xylazine is an alpha 2 adrenergic non-narcotic CNS depressant with muscle relaxant properties. It is widely used in ruminants where it is accompanied by recumbancy, hypotension and bradycardia (Clarke and Hall, 1969; Richard et al., 1974, Knight, 1980; Ahmed et al., 1996). In the camel, xylazine was reported to give good sedation (Bauditz 1972; Custer et al., 1977), and was superior when compared with other CNS depressing drugs (Khamis et al., 1973). It was proved to be safe and the drug of choice for inducing CNS depression in the camel (Sharma et al., 1982; Higgins and Kock, 1984). Pershin et al. (1980) recommended the use of 0.4 mg/kg of xylazine intramuscularly for short surgical procedures in dromedaries.

The availability of a range of antagonists for xylazine greatly improved the chances of safer administration of the drug to different animal species (Hsu, 1981; 1982; 1983; Hsu et al., 1981, 1985; McNeel and Hsu, 1984). Various antagonists were used to reverse xylazine depressant effects, especially yohimbine and tolazoline, which are alpha adrenergic blocking agents (Hatch et al., 1982; Kitzman et al., 1982; Wallner et al., 1982; Goldburg and Robertson, 1983). Antagonism of xylazine sedation in camel was studied by Ahmed et al. (1996) who reported that the decrease in respiratory rate, bradycardia, increased blood glucose and blood cell counts could be reversed by tolazoline injection given at the rate of 1.5 mg/kg body weight. Yohimbine was specifically recommended to antagonize the effect of xylazine in many species of animals (Hsu, 1981 b, 1983; Hsu et al., 1981, Hatch 1983 and Jensen, 1985). The results about which is more potent were

contradictory (Zingoni et al., 1982 and Guard and Schwark, 1984; Takase et al., 1986). The effect of yohimbine antagonism to xylazine in camels is not well documented in the literature.

Antagonism of xylazine is needed to counteract the inadvertent overdose that might occur because of the false gross estimation of the animal weight. In this paper the effects of xylazine CNS depression in camels as well as its reversal by tolazoline and yohimbine is reported.

MATERIAL and METHODS

Twelve male camel calves were allocated randomly to three groups of four animals each. The animals were restrained in a sitting position one hour before experimenting to avoid the effect of stress.

All the animals were injected with xylazine at a dose of 0.5 mg/kg body weight. Ten minutes later, group 1 camels were injected intravenously (iv) with 5 ml of saline, group 2 animals were injected iv 1.5 mg/kg tolazoline and group three camels were injected iv with 0.25 mg/kg yohimbine. The animals were bled before and after ten minutes from xylazine injection.

Heart rate, respiratory rate and ruminal movements per minute were recorded before xylazine injection and after 10, 20, 30, 45, 60 and 90 minutes. The heart rate was measured by using a stethoscope, the respiratory rate by observing abdominal wall movement and the ruminal movements by using a stethoscope at the lumber fossa on the left side of the animal.

RESULTS

The animals began to be calm within 3 minutes after xylazine injection. All animals were in lateral recumbency 6 to 7 minutes post-xylazine injection . The animals of group 1 which were not treated with xylazine antagonists showed no reaction to deep pin pricks for 30 minutes. The light reflex was very weak but the corneal and anal reflexes were weak for 25 minutes after xylazine injection. The CNS depression of xylazine was reversed in 6-7 minutes after administration of tolazoline and the animals turned to sternal recumbency. Injection of yohimbine to the camels of group 3 resulted in quick recovery and the animals regained sternal recumbency within 2-4 minutes after yohimbine administration.

After the iv administration of xylazine in camels at a dose rate of 0.5 mg /kg body weight, the heart rate decreased sharply within 10

minutes (Fig. 1). The rate began to increase slightly after 45 minutes and was apparent after 90 minutes. When tolazoline at a dose rate of 1.5 mg/ kg body weight was iv injected 10 minutes after xylazine in the animals of group 2, the heart rate was markedly increased, but did not reach its value before xylazine injection. The improvement of the heart rate was much more pronounced when yohimbine at a dose rate of 0.25 mg/ kg body weight was injected intravenously 10 minutes after xylazine administration. The heart rate became near the original values within 50 minutes after yohimbine injection.

The respiratory rate decreased markedly within 20 minutes after xylazine administration, but began to increase after 30 minutes (Fig. 2). Injection of tolazoline or yohimbine 10 minutes after xylazine administration guarded against the sharp decrease of the respiratory rate. The improvement was much more pronounced with the use of yohimbine.

The ruminal movements decreased sharply to stop completely within 30 minutes after the intravenous injection of xylazine at a dose rate of 0.5 mg/ kg body weight in camels (Fig. 3). Ruminal motility remained decreased, but with slight improvement till 90 minutes after xylazine administration. Injection of tolazoline did not counteract the decrease of ruminal movements produced by xylazine but did protect against ruminal stasis. Improvement of ruminal motley was more pronounced with yohimbine which counteract the depressant effect of xylazine.

DISCUSSION

Xylazine induced CNS depression is mediated by alpha 2 adrenoreceptors (Hsu, 1981b), and thus should be antagonized by alpha 2 adrenoreceptor antagonists such as tolazoline or yohimbine (Zingoni et al., 1982; Doherty et al., 1986 and Hsu et al., 1987).

While, CNS depression began within three minutes after the intravenous administration of xylazine in camel in a dose rate of 0.5 mg/kg body weight, deep calming where apparent within 6 to 7 minutes and lasted for 25 to 30 minutes. Tolazoline and yohimbine could reverse xylazine CNS depression in camels within 2 to 7 minutes.

While xylazine produced bradycardia and decrease in the respiratory rate were reversed within 10 minutes after tolazoline and yohimbine administration, the improvement of rumen motility took 80 minutes to be apparent.

Although both yohimbine and tolazoline could antagonise xylazine, yohimbine effect was more pronounced than tolazoline to reverse the depressant effect of xylazine in camels. The results about which is more potent were contradictory (Zingoni, et al., 1982 and Guard and Scwark, 1984; Takase, et al., 1986. Hsu, et al. (1987) reported that the reversal effects of tolazoline and yohimbine on xylazine- induced bradycardia did not differ significantly. The difference between his and our results may be due to the increase in the dose of tolazoline and the decrease in the dose of yohimbine in the present study.

The results of the present study indicate that both tolazoline and yohimbine at the doses studied have a marked antagonistic effect on the CNS depression, bradycardia, respiratory depression and decreased ruminal motility. These antagonistic effects suggest that yohimbine and tolazoline would be useful antidot for xylazine overdose in camels.

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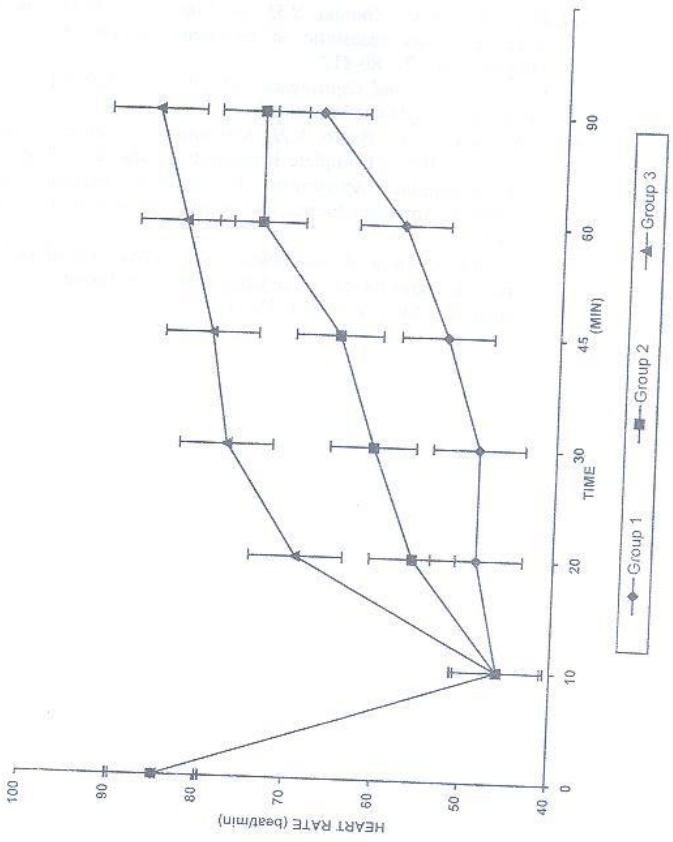

Fig. 1. Changes in heart rate before and after xylazine and yohimbine or tolazoline injection

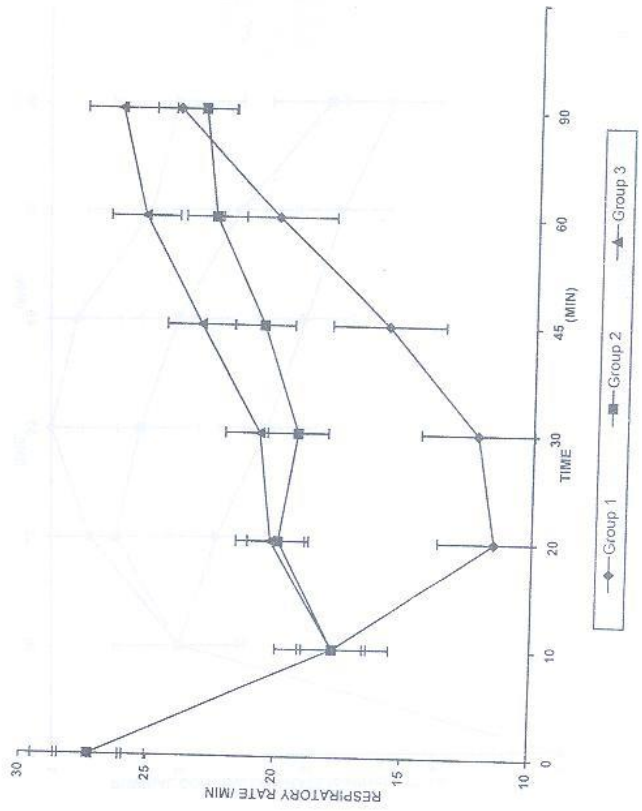

Fig. 2. Changes in respiratory rate before and after xylazine and yohimbine or tolazoline injection

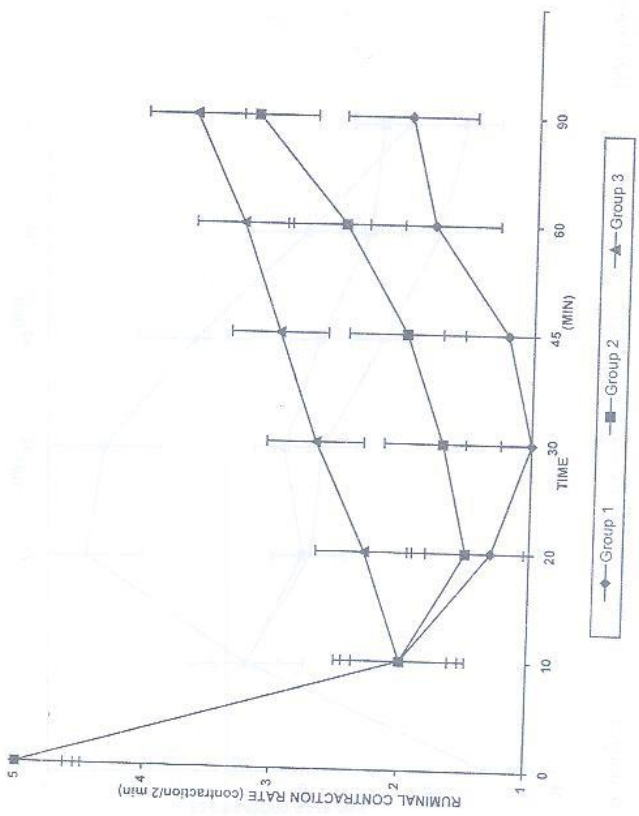

Fig. 3. Changes in ruminal movements before and after xylazine and yohimbine or tolazoline injection

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